REMARKS

Interview Summary

Pursuant to 37 CFR §1.133(b), Applicants acknowledge with appreciation the telephonic interview with the Examiner on December 13, 2007 during which the foregoing claim amendments were discussed, as well as the claim rejections under 35 U.S.C. §112, first paragraph, regarding enablement.

Claim Amendments

Applicants note with appreciation that claims 3, 5-11, 13, 15, 19-21, 55, 56, 67, and 99-102 have been indicated allowable. Applicants also note with appreciation that the Examiner has searched and examined each of the antibody sequences specifically recited in the claims, as requested by Applicants in response to the previous restriction requirement.

Claims 2-11, 13, 15, 17, 19-21, 40-50, 53-56, 67, and 99-102 are pending. Claims 40-50 have been canceled without prejudice. Claim 17 has been amended. New claims 109-115 have been added.

Claim 17 has been amended to specify that the isolated monoclonal antibody "binds to human CD25." Support for this amendment can be found throughout the application as originally filed.

New claims 109-115 are drawn to isolated antibodies which bind human CD25 and include the particular variable region sequences recited in allowable claims 99-102. Support for new claims 109-115 can be found throughout the application as originally filed.

The foregoing claim amendments should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite prosecution of the application. Applicants reserve the right to pursue claims to the canceled subject matter, or any subject matter which they are entitled to claim, in this or a separate application. No new matter has been added.

Rejection of Claims 2, 4, 40-50, 53, and 54 Under 35 U.S.C. §112, First Paragraph

Claims 2, 4, 40-50, 53, and 54 are rejected as not being enabled. Applicants respectfully disagree. However, to expedite prosecution, claims 40-50 have been canceled without prejudice.

With respect to claims 2, 4, 53, and 54, the Examiner notes that these claims are directed to antibodies comprising various isotypes. The Examiner asserts, however, that "Applicants have characterized *only* four (4) anti-human CD25 antibody clones ... expressed from the germline gene sequence from HCo mice ... and **all were IgG1, kappa** ..." (emphasis in original). The Examiner relies on Davis *et al.* (1999) and Gallo *et al.* (2000) and argues that "one skilled in the art could not have predicted or would have expected to obtain any Ig class of human anti-CD25 antibody having structural diversity from a transgenic mouse and meeting all the functional properties for a human CD25 antibody as broadly encompassed by the claims."

Applicants respectfully traverse this rejection. Claims 2, 4, 53, and 54 are drawn to various isotypes of isolated human monoclonal antibodies which bind to human CD25 and include particular variable region sequences (e.g., all six CDR sequences). Such antibodies, which are not limited to those produced by transgenic mice (as stated by the Examiner in paragraph 14 of the preset office action), are fully enabled. Indeed, once provided with the variable region sequence information (as claimed), antibodies of varying classes could have been produced without undue experimentation by recombinant technology at the time the present application was filed.

For example, as taught by Applicants in the present specification (see, e.g., page 23, lines 18-23):

> The light and heavy chain variable regions of the antibodies described herein can be used to create full-length antibody genes of any antibody isotype by inserting them into expression vectors already encoding heavy chain constant and light chain constant regions of the desired isotype such that the V_H segment is operatively linked to the C_H segment(s) within the vector and the V_L segment is operatively linked to the C_L segment within the vector. Additionally or alternatively, the recombinant expression vector can encode a signal peptide that facilitates secretion of the antibody chain from a host cell.

Applicants further teach the construction of particular plasmids for the expression of various heavy chain isotypes, or for the expression of antibodies comprising lambda light chains, as well as isotype-specific chromatographic methods for separating such antibodies (see, pages 27-28).

In addition, prior to the present filing date, methods for generating antibodies having different isotypes, based on a fixed variable region sequence, were known in the art and could

have been performed without undue experimentation; see, for example, Preston *et al.* (1998) Infection and Immunity 66(9):4137-4142, Yarnold and Fell (1994) Cancer Research 54:506-512, Morrison *et al.* (1994) PNAS USA 88:6851-6855, and Boel *et al.* (2000) J. of Immunological Methods 239:153-166 (enclosed herewith as Appendices A, B, C, and D, respectively).

Specifically, Preston *et al.* describe using the heavy and light chain variable regions of a murine monoclonal antibody that binds *Pseudomonas aeruginosa* to generate a series of chimeric antibodies with identical variable regions. As described in the abstract, the murine variable regions gene segments were cloned into an immunoglobulin cDNA expression vector that contained human kappa light chain and IgG1 constant regions. Preston *et al.* further describe replacing the IgG1 heavy chain constant region with a human IgG2, IgG3, IgG4, or IgA1 heavy chain constant region and the successful production of the resulting antibodies in CHO cells. Similarly, Yarnold and Fell describe conversion of murine hybridoma cell lines expressing IgG3, IgG1 or IgG2a heavy chains into chimeric IgG1 producers. Morrison *et al.* describe joining the variable region genes of a mouse antibody-producing cell line to a human immunoglobulin IgG1 or IgG2 constant region gene and the successful production of such antibodies. Boel *et al.* generated functional human monoclonal antibodies of all isotypes from a phage display library-derived single-chain Fv antibody fragments. As described in the abstract, a scFv fragment specific for sheep red blood cells was isolated from a semi-synthetic phage antibody display library was used to produce human monoclonal antibodies of IgM, IgG1. IgG2, IgG3, IgG4, IgA1, IgA2m(I), and IgE isotype *in vitro* in stably transfected cells.

Accordingly, based on the present specification which provides an in-depth teaching of how to generate antibodies of various isotypes based on a known variable region sequence, and prior publications which provide evidence that the requisite techniques were well-known and within the skill in the art, claims 2, 4, 53, and 54 are fully enabled.

CONCLUSION

If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

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Respectfully submitted,

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